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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,555	03/30/2004	Matthew D. Linnik	252312008000	7418

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MORRISON & FOERSTER LLP
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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/814,555	LINNIK ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *7-9 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10-19 and 23-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/6/05 & 11/22/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to papers filed November 22, 2006. Applicant's response to restriction requirement of September 22, 2006 has been entered. No claims were canceled, amended, or newly added. Claims 1-26 are pending in the application.

Election/Restrictions

Applicants' species election of "LJP 394", consisting of AHAB-TEG non-immunogenic valency platform and the double-stranded sequence $(CA)_{10}$.$(TG)_{10}$ epitope, as defined in paragraph 177 of the specification, is acknowledged. Accordingly, claims 7-9 and 20-22 are hereby withdrawn from further consideration, as drawn to non-elected species of the invention.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). As the species restriction is still deemed proper, the requirement for restriction is maintained and hereby made FINAL

Elected claims 1-6, 10-19 and 23-26 are under current examination.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 5, 6, 16, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 5, 6, 16, 18 and 19 are unclear. The claims contain the recitation "wherein the double stranded DNA epitopes are polynucleotides". However, it is not clear what the polynucleotide is intended to further limit, as a polynucleotide encompasses and is broader than the double stranded DNA.

Response to Claim Rejections - 35 USC § 112-Scope of Enablement

Claims 1-6, 10-19 and 23-26 are rejected under 35 U.S.C.§112, first paragraph, because the specification, while being enabling for a method of treating systemic lupus erythematosus (SLE) and reducing renal flare in a subpopulation of human individuals characterized by having high affinity IgG antibodies to LJP-394, comprising administering to said individuals an effective amount of LJP-394 to reduce the levels of anti-dsDNA antibodies, does not reasonably provide an enablement for a method of treating SLE and reducing the risk of renal flare in any human individual following the administration of LJP-394, resulting in an indefinitely sustained reduction id anti-dsDNA antibody, as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is based on the absence of an enabling disclosure for the method of treating SLE and reducing the risk of renal flare by administering an effective amount of LJP-394 to any human individual with the disease and resulting in a sustained reduction of anti-dsDNA antibody for an indefinite period of time. In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by Applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404:

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

MPEP § 2164.04 states: "[W]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection."

When given their broadest reasonable interpretation, in view of the as filed specification, the claims encompass methods of treating SLE and reducing the risk of renal flare in any human individual having SLE. However, the specification does not provide an enabling disclosure for the methods of treating SLE in any human population following the administration of an effective amount of LJP-394.

The specification teaches the results obtained from several phase II/III clinical trials wherein SLE patients were treated at various dosing regimens with LJP 394 (Examples 1-7, pp. 69-81). These studies included clinical trials 90-05 (Example 2), wherein 100 mg of LJP 394 was administered for 16 weeks (induction period), followed by alternating 8 weeks off and 12 weeks of treatment with 50 mg of LJP 394 (maintenance period) for a total period of 60 weeks (p. 70). The patients were segregated into "high affinity" and "low affinity" subgroups (Example 1) or an intent-to-treat population (defined by high affinity antibodies to LJP 394) in Example 3 (clinical study 90-09). The studies concluded that patients with sustained reductions in anti-dsDNA have fewer renal flares (Example 5). It is apparent from the preceding analyses that the patient population that responded to the treatment regimens with LJP 394 in a statistically significant manner was limited to the sub-population of SLE patients having high affinity antibodies to LJP 394. Further the sustained reduction in antibodies to ds-DNA as depicted in Figures 3 and 4 are limited to the clinical study period and wherein LJP 394 is administered throughout.

The results of the phase II/III 90-05 clinical trials are summarized in the prior art of Wallace (Exp. Opin. Invest. Drugs 10:111-117; 2001; of record). The author states that an interim analysis of the study with primary end-point of delayed renal flares, and secondary objective of reduced anti-ds-DNA antibody concentration and reduced symptoms of SLE, showed no significant differences in the distribution of time to renal flare between active and placebo groups (first column, p. 115). However, when the data from the study was reanalyzed, removing the study cohort without the high affinity

antibodies from analysis, now LJP 394 decreased the time to renal flare (second column, p. 115). The authors conclude that LJP 394 displays disease-suppressing effects in patients with serious lupus who have high levels of anti-ds-DNA and high-affinity antibodies to the drug, that includes 20-40% of all SLE patients (second column, p. 116). Therefore, the results of the clinical studies may not be extended to all SLE patients and a sustained reduction in anti-ds-DNA antibodies in a sub-population of SLE patients has not been demonstrated for an indefinite period of time.

The guidance provided by the specification amounts to an invitation for the skilled Artisan to try and follow the disclosed instructions to make and use the claimed invention. The specification merely discloses methods for treating SLE in a sub-population of SLE patients characterized by high levels of anti-ds-DNA and high-affinity antibodies to LJP 394 for a specified period of drug administration.

The detail of the disclosure provided by Applicant, in view of the prior art, must encompass a wide knowledge, so that the Artisan of skill would be able to practice the invention as claimed by Applicant, without undue burden being imposed on such Artisan. This burden has not been met because it would require undue experimentation to treat SLE and reduce renal flare in any human population having SLE and achieve a sustained reduction of anti-dsDNA antibody in said patients for an indefinite period, absent continued administration of the drug, as claimed in the instant application.

Therefore, in view of the art recognized high level of unpredictability of treatment of SLE, and the large quantity of research required to define these unpredictable variables, and the lack of guidance provided in the specification regarding the indefinite and sustained reduction in anti-ds-DNA antibodies in any population of SLE patients, it is the position of the examiner that it would require undue experimentation for one of skill in the art to practice the scope of the invention as broadly claimed. Hence, absent a strong showing by Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by Applicant is not enabled.

New Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 10-19 and 23-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Wallace (Exp. Opin. Invest. Drugs 10:111-117; 2001; or record).

The claims encompass a method of treating SLE and reducing the risk of renal flare in SLE human individual, comprising administering to said individual an effective amount of LJP-394 (elected species of agent comprising a dsDNA epitope).

Wallace teaches the clinical and pharmacological results from human clinical trials, wherein LJP-394 (composed of four double-stranded oligodeoxynucleotides attached to a central branched platform, that acts as an anti-anti-dsDNA B-cell toleragen, Figure 1), was administered intravenously as a weekly dose of 100 mg to patients with lupus nephritis. The results showed clinical benefits in patients with high affinity IgG antibodies to LJP-394, that included increased time to renal flares and reduced number of renal flares and lower anti-ds-DNA antibody levels (Abstract). Wallace further teaches that in patients treated with creatinines, anti-ds-DNA antibody was reduced by a mean of 29% (first and second columns, bridging, p. 115).

While Wallace does not present results showing a sustained reduction of anti-dsDNA antibody in the individual, this limitation is an inherent property of the dose and treatment regimen of SLE patients with LJP-394. There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. The clinical trial results summarized by Wallace involved the identical chemical composition of the instantly claimed methods. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). As stated in MPEP

2112: The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." In re Napier, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir.1995) (affirmed a 35 U.S.C. 103 rejection based in part on inherent disclosure in one of the references). See also In re Grasselli, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983).

Moreover, "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Therefore by teaching all the limitations of claims 1-2, 10-11, and 37-44, Wallace anticipates the instant invention as claimed.

Conclusion

Claims 1-6, 10-19 and 23-26 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

Fereydoun G. Sajjadi, Ph.D.
Examiner, AU 1633

AU 1633